

# Figure 1

PG5 PTH(1-9)/(Gly)PTH(15-31)

1  
A-V-S-E-I-Q-L-M-H-g-g-g-g-g-L-N-S-M-E-R-V-E-W-L-R-K-K-L-Q-D-V-NH2<sup>31</sup>

SEQ ID NO: 9

1 GCUGUUUCCG AAUCCAGCU GAUGCACGGU GGUGGUGGUG GUCUGAACUC

51 CAUGGAACGU GUUGAAUGGC UGCGUAAAAA ACUGCAGGAC GUU SEQ ID NO: 14

PG7 PTH(1-9)/(Gly)PTH(17-31)

1  
A-V-S-E-I-Q-L-M-H-g-g-g-g-g-g-g-S-M-E-R-V-E-W-L-R-K-K-L-Q-D-V-NH2<sup>31</sup>

SEQ ID NO: 11

1 GCUGUUUCCG AAUCCAGCU GAUGCACGGU GGUGGUGGUG GUGGUGGUUC

51 CAUGGAACGU GUUGAAUGGC UGCGUAAAAA ACUGCAGGAC GUU SEQ ID NO: 15

PG9 PTH(1-5)/(Gly)PTH(15-31)

1  
A-V-S-E-I-g-g-g-g-g-g-g-g-g-L-N-S-M-E-R-V-E-W-L-R-K-K-L-Q-D-V-NH2<sup>31</sup>

SEQ ID NO: 13

1 GCUGUUUCCG AAUCCGUGG UGGUGGUGGU GGUGGUGGUG GUCUGAACUC

51 CAUGGAACGU GUUGAAUGGC UGCGUAAAAA ACUGCAGGAC GUU SEQ ID NO: 16

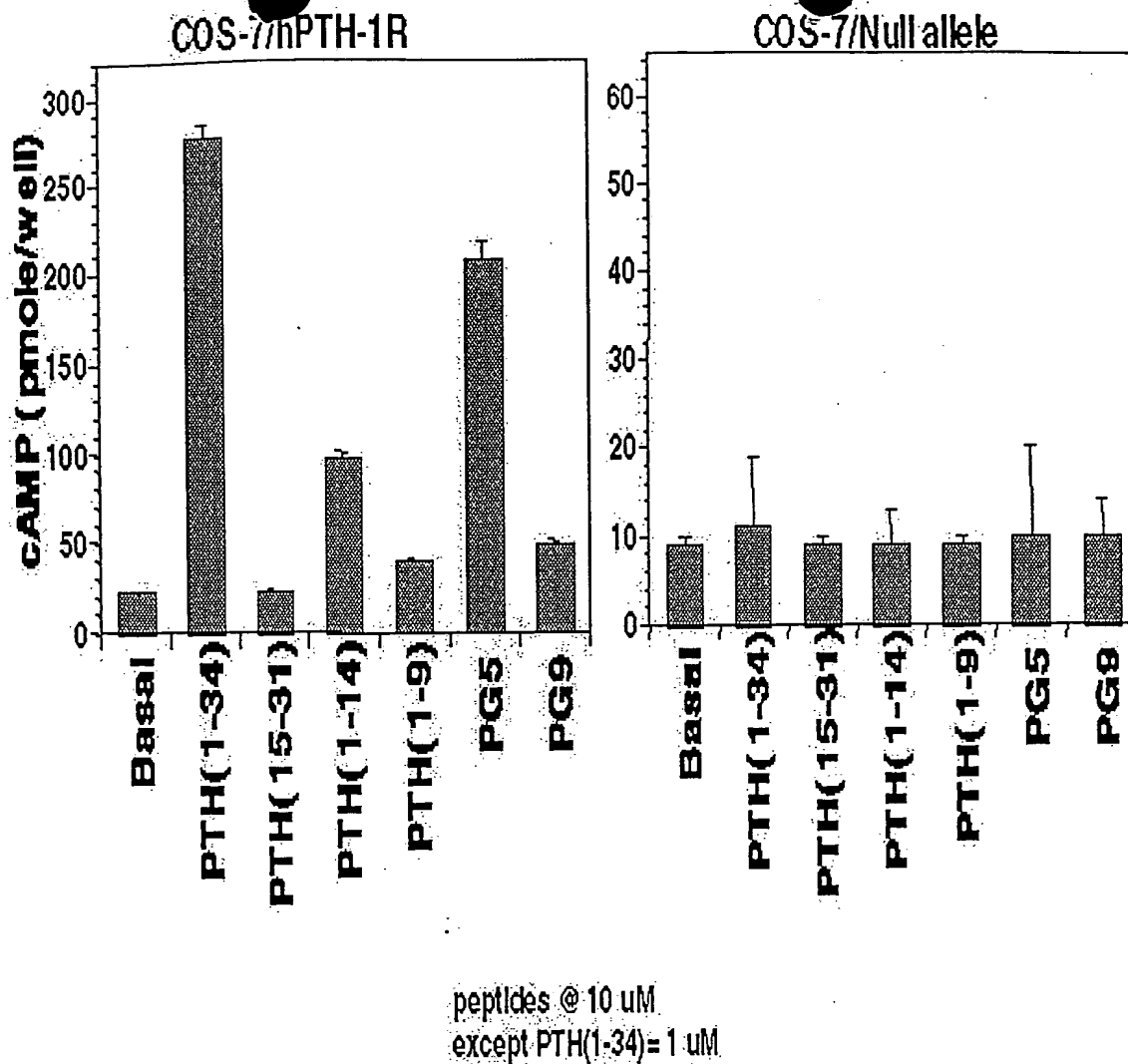
Figure 2

12-28-98

hpth	1	SVSEI QLMNLTCKHL NSMERVENLR KTLQDVHNE	SEQ ID NO: 17
hpthrpi	AVSEH	QLTHDKGKSI QDIRBREELH HLAIEIHIA	SEQ ID NO: 18
hpacapi	HSDGI	FTDSYSRKRQ QMAVKYILAA VLGRKYKOR VNK	SEQ ID NO: 19
hw4p	1	HSDAV FTDNYTRLRK QMAVKYILNS ILN	SEQ ID NO: 20
hgze	1	XADAI FTNSYRKVLG QLSARKLLOD IMSR	SEQ ID NO: 21
hphm	1	HADGV FTSDEFSKLLG QLSAKKYLES IM	SEQ ID NO: 22
hglpi	7	HAEGT FTSDEVSSYLE GQAACEFLAN LVKGRG	SEQ ID NO: 23
hglucagon	1	HSQGT FTSDESKYLD SRBAQDFVOM LMNT	SEQ ID NO: 24
gip	1	YAEGT FISDYSLAND KIHOODEVNMT LLAQKGKN DMKHNITQ	SEQ ID NO: 25
hsecretin	1	HSDDT FTSELISRLRE GARLQRLLQG IV	SEQ ID NO: 26
hcalcitonin	1	CGNLS TCMLGTYTOD ENKEHTEPQT AIGVGAP	SEQ ID NO: 27
hcgyp-2	1	ACNTA TCVTTRLAGL ILSRGGMVKS NEVPITNGSKAF	SEQ ID NO: 28
hcgrpi1	ACDTA	TCVTTRLAGL ILSRGGVKN NEVPITNGSKAF	SEQ ID NO: 29
hamyl1n	1	KCNTA TCATQRIANF LVHSSNFGA ILSTNVGSNTX	SEQ ID NO: 30
hadrenomedu	1	GCRFG TCTVOQLAHQ IYQETDKKD NVAPRSKISPQ	SEQ ID NO: 31
horf	1	SEERP ISDLTFELL REVELEMARAB QLAQOASHNRKIMEII	SEQ ID NO: 32
sauvagine	1	EEBPI SIDISLELTR KMIEIEKOEK EKQOAMNRLIDTI	SEQ ID NO: 33
msdh	1	TGAQS LISVAPLDVL RQRLMEINR RMRELQSGRIQQNRQLTISI	SEQ ID NO: 34
Maxad1lin	1	CDAIC QERKAIDCQ KOAHHSNVLQ TSVOPTAITSMNTSQLPNGSNVFKECMKQKKKEESSGK	SEQ ID NO: 35

Figure 3

A



B

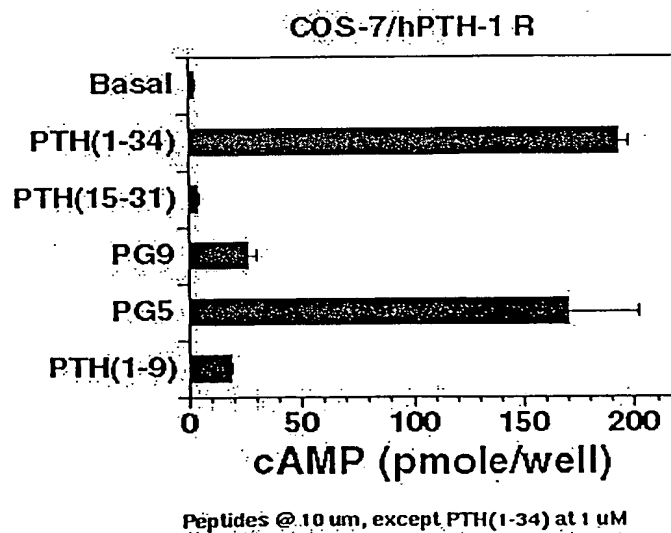
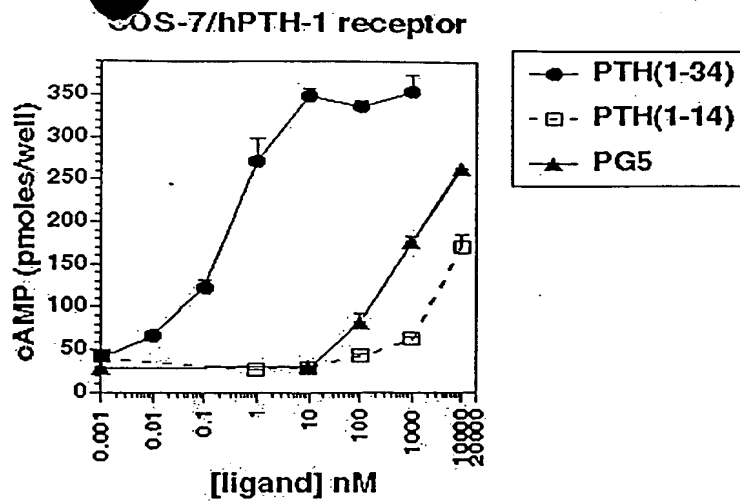
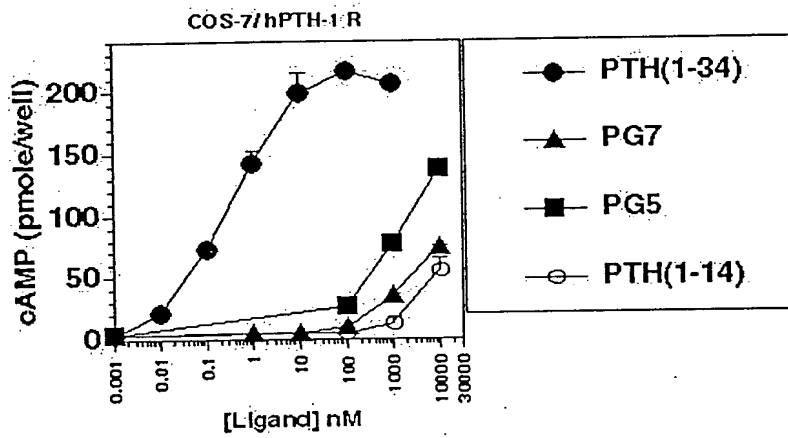


Figure 4

A



B



C

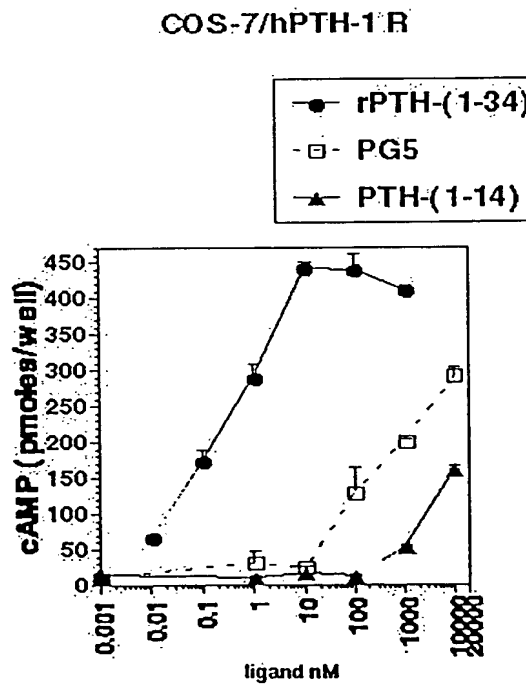


Figure 5

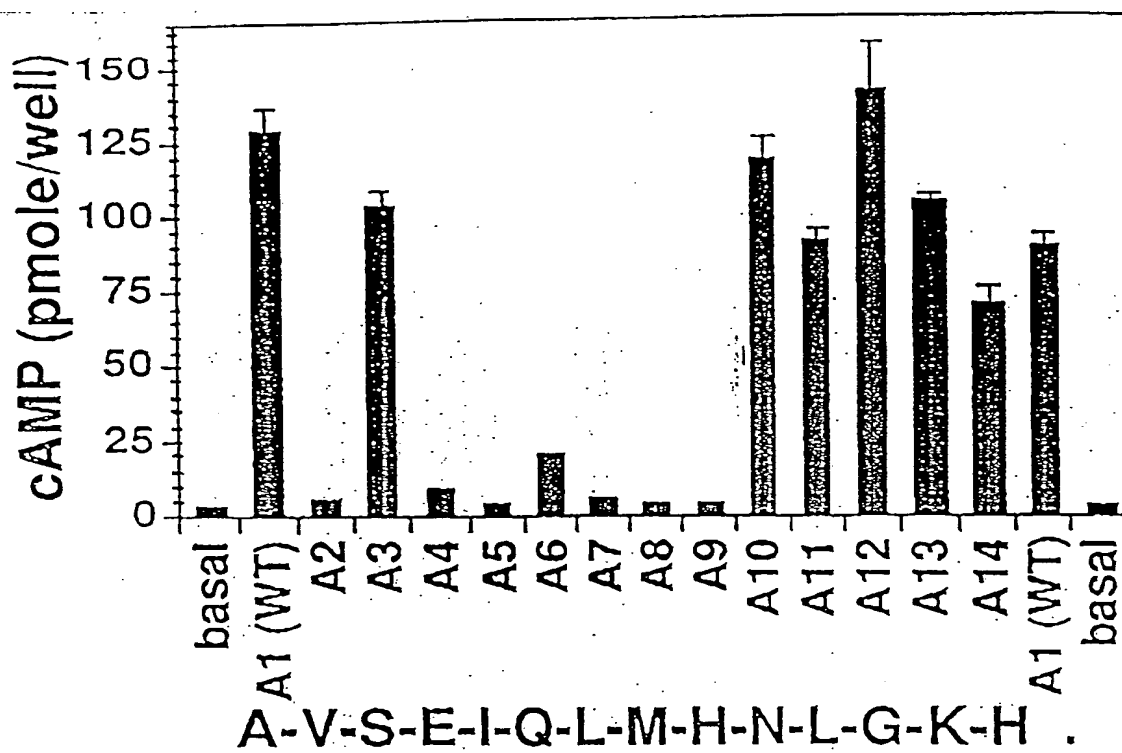


Figure 6

Alanine Scan of PTH(17-31)			
native PTH(17-31)		Binding IC <sub>50</sub> ( $\mu$ M) $1.0 \pm 0.1$	n 14
Position	Substitution		
17	Ser→Ala	$1.5 \pm 0.2$	14
18	Met→Ala	$1.5 \pm 0.3$	5
19	Glu→Ala	$0.7 \pm 0.1$	5
20	Arg→Ala	$90.5 \pm 50.0$	5
21	Val→Ala	$1.7 \pm 0.2$	5
22	Glu→Ala	$0.6 \pm 0.2$	8
23	Trp→Ala	> 100	8
24	Leu→Ala	$67.5 \pm 14.3$	5
25	Arg→Ala	$3.8 \pm 0.9$	5
26	Lys→Ala	$8.3 \pm 1.2$	5
27	Lys→Ala	$1.1 \pm 0.1$	5
28	Leu→Ala	$9.9 \pm 1.4$	5
29	Gln→Ala	$0.9 \pm 0.1$	5
30	Asp→Ala	$1.1 \pm 0.2$	5
31	Val→Ala	$3.8 \pm 0.6$	5
<p>Competition binding analysis for each PTH(17-31) peptide analog was performed in COS-7 cells transfected with PTH-2 receptors. IC<sub>50</sub> is the dose of a peptide analog which inhibited by 50% the binding of <sup>125</sup>I-rPTH(1-34). Each analysis was performed the number of times indicated(n).</p>			

# Figure 7

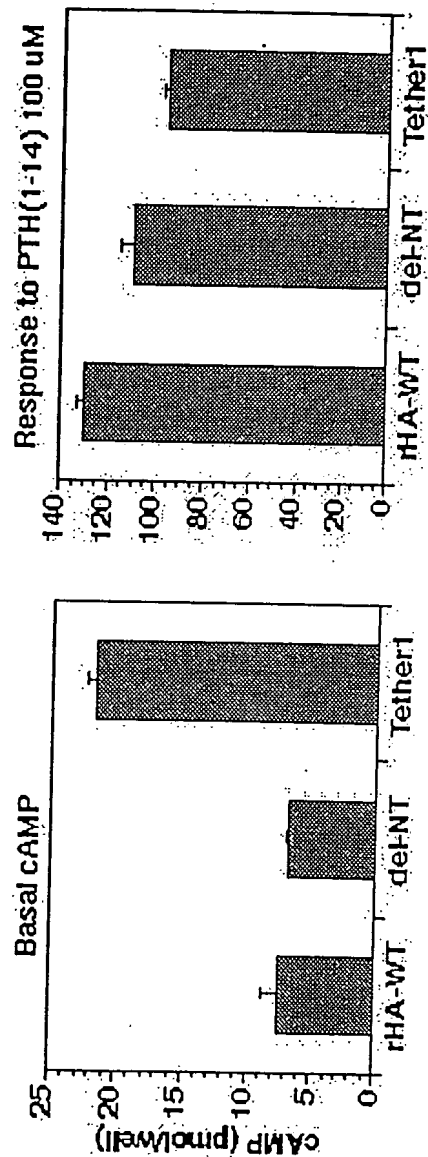
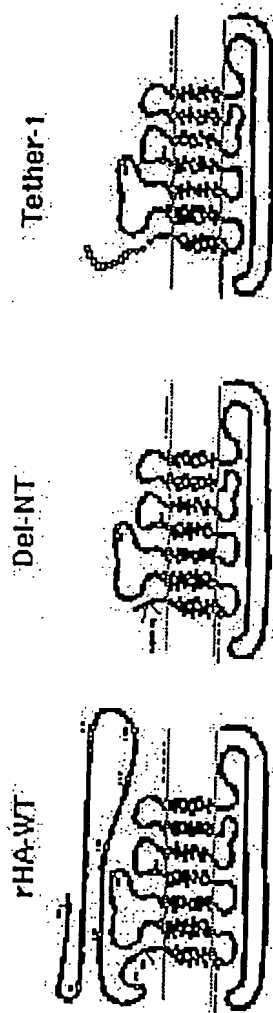
MAP of: tether-1.seq from: 2319 to: 3698  
 PTH(1-9) linked to Glu-182 of rat receptor. insert immediately after  
 Tyr23 cleavage site. December 29, 1998 15:27 ..

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ATGGGGGGCCGCCCGGATCGCACCCAGCCTGGCGCTCCTACTCTGCTGCCCAGTGCTCAGC
M G A A R I A P S L A L L L C C P V L S
TCCGCcTATGCGGUUCCGAAAUCCAGCUGAUGCACggcggaggaggcGAGGTATTTGAC
S A Y A V S E I Q L M H G G G G E V F D
CGCCTAGGCATGATCTACACCGTGGGATACTCCATGTCTCTCGCCTCCCTCACGGTGGCT
R L G M I Y T V G Y S M S L A S L T V A
GTGCTCATCCTGGCCTATTTTAGCGGGCTGCACTGCACGCGCAACTACATCCACATGCAC
V L I L A Y F R R L H C T R N Y I H M H
ATGTTCTGTCTGTTTATGCTGCGCGCCGCGAGCATCTTCGTGAAGGACGCTGTGCTCTAC
M F L S F M L R A A S I F V K D A V L Y
TCTGCTTCACGCTGGATGAGGCGGAGCGCTCACAGAGGAAGAGTTGCACATCATCGCG
S G F T L A Y F R R L T E E E L H I I A
CAGGTGCCACCTCCGCGCGGCGCTGCCGCGTAGGCTACGCTGGCTGCCGCGTGGCGGTG
Q V P P P P A A A A V G Y A G C R V A V
ACCTTCTTCTCTACTTCTGGCTACCAACTACTACTGGATcCTGGTGGAGGGGCTGTAC
T F F L A Y F L A T N Y Y W I L V E G L Y
TTGCACAGCCTCATCTTACATGGCCTTTTTCTCAGAGAAGAAGTACCTGTGGGCTTCACC
L H S L I F M A F F S E K K Y L W G F T
ATCTTTGGCTGGGGTCTACCGGCTGTCTTCTGCTGGCTGTGTGGGTGCGGTGTACAGCAACC
I F G W G L P A V F V A V W V G V R A T
TTGGCCAAACATGGGTGCTGGGATCTGAGCTCCGGGCACAAGAAGTGGATCATCCAGGTG
L A N T G C W D L S S G H K K W I I Q V
CCCATCCTGGCATCTGTTGTGCTCAACTTCATCCTTTTATCAACATCATCCGGGTGCTT
P I L A S V V L N F I L F I N I I R V L
GCCACTAAGCTTCGGGAGACCAATGCGGGCGGTGTGACACCAGGCAGCAGTACCGGAAG
A T K L R E T N A G R C D T R Q Q Y R K
CTGCTCAGGTCCACGTTGGTGCTCGTGCCGCTCTTTGGTGTgCACTACACCGTCTTCATG
L L R S T L V L V P L F G V H Y T V F M
GCCTTGCGGTACACCGAGGTCTCAGGGACATTGTGGCAGATCCAGATGCATTATGAGATG
A L P Y T E V S G T L W Q I Q M H Y E M
CTCTTCAACTCCTTCCAGGGATTTTTTGTGTCATATACTGTTTCTGCAATGGTGAG
L F N S F Q G F F V A I I Y C F C N G E
GTGCAGGCAGAGATTAGGAAGTCATGGAGCCGCTGGACACTGGCGTTGGACTTCAAGCGC
V Q A E I R K S W S R W T L A L D F K R
AAAGCACGAAGTGGGAGTAGCAGCTACAGCTATGGCCCAATGGTGTCTCACACGAGTGTG
K A R S G S S S Y S Y G P M V S H T S V
ACCAATGTGGGCCCCCGTGCAGGACTCAGCCTCCCCCTCAGCCCCCGCTGCCTCCTGCC
T N V G P R A G L S L P L S P R L P P A
ACTACCAATGGCCACTCCCAGCTGCCTGGCCATGCCAAGCCAGGGGCTCCAGCCACTGAG
T T N G H S Q L P G H A K P G A P A T E
ACTGAAACCCTACCAGTCACTATGGCGGTTCCCAAGGACGATGGATTTCCTTAACGGCTCC
T E T L P V T M A V P K D D G F L N G S
TGCTCAGGCCTGGATGAGGAGGCTCCGGGTCTGCGCGGCCGCTCCATTGTTGCAGGAA
C S G L D E E A S G S A R P P P L L Q E
GGATGGGAAACAGTCATGTGA SEQ ID No: 36
G W E T V M * SEQ ID No: 37

```

Figure 8





# Figure 9

MAP of: Tether-1C, Seq check: 6795 from: 2319 to: 3326  
Stop codon at 481 added to Tether-1

```

a   ATGGGGGGCCGCCCCGATGCGACCCAGCCTGGCGCTCCTACTCTGCTGCCAGTGCTCAGC
    M G A A R I A P S L A L L L C C P V L S -

a   TCCGCCcTATGCGGUUCCGAAAUCCAGCUGAUGCACggcggaggaggcGAGGTATTTGAC
    S A Y A V S E I Q L M H G G G G E V F D -

a   CGCCTAGGCATGATCTACACCGTGGGATACTCCATGTCTCTCGCCTCCCTCACGGTGGCT
    R L G M I Y T V G Y S M S L A S L T V A -

a   GTGCTCATCCTGGCCTATTTTAGGCGGCTGCAC TG CACGCGCAACTACATCCACATGCAC
    V L I L A Y F R R L H C T R N Y I H M H -

a   ATGTTCTGTGCTTTATGCTGCGCGCCGCGAGCATCTTCGTGAAGGACGCTGTGCTCTAC
    M F L S F M L R A A S I F V K D A V L Y -

a   TCTGGCTTCACGCTGGATGAGGCCGAGCGCCTCACAGAGGAAGAGTTGCACATCATCGCG
    S G F T L D E A E R L T E E E L H I I A -

a   CAGGTGCCACCTCCGCCGCGCGCTGCCGCGTAGGCTACGCTGGCTGCCGCGTGGCGGTG
    Q V P P P P A A A A V G Y A G C R V A V -

a   ACCTTCTTCTCTACTTCTGGCTACCAACTACTACTGGATcCTGGTGGAGGGGCTGTAC
    T F F L Y F L A T N Y Y W I L V E G L Y -

a   TTGCACAGCCTCATCTTCATGGCCTTTTTCTCAGAGAAGAAGTACCTGTGGGGCTTCACC
    L H S L I F M A F F S E K K Y L W G F T -

a   ATCTTTGGCTGGGGTCTACCGGCTGTCTTCGTGGCTGTGTGGGTGGGTGTGAGAGCAACC
    I F G W G L P A V F V A V W V G V R A T -

a   TTGGCCAACTGCGGTGCTGGGATCTGAGCTCCGGGCACAAGAAGTGGATCATCCAGGTG
    L A N T G C W D L S S G H K K W I I Q V -

a   CCCATCCTGGCATCTGTTGTGCTCAACTTCATCCTTTTTATCAACATCATCCGGGTGCTT
    P I L A S V V L N F I L F I N I I R V L -

a   GCCACTAAGCTTCGGGAGACCAATGCGGGCCGGTGTGACACCAGGCAGCAGTACCGGAAG
    A T K L R E T N A G R C D T R Q Q Y R K -

a   CTGCTCAGGTCCACGTTGGTGTGCTGCGGCTCTTTGGTGTgCACTACACCGTCTTCATG
    L L R S T L V L V P L F G V H Y T V F M -

a   GCCTTGCCGTACACCGAGGTCTCAGGGACATTGTGGCAGATCCAGATGCATTATGAGATG
    A L P Y T E V S G T L W Q I Q M H Y E M -

a   CTCTTCAACTCCTTCCAGGGATTTTTTGTGGCCATCATATACTGTTTCTGCAATGGTGAG
    L F N S F Q G F F V A I I Y C F C N G E -

a   GTGCAGGCAGAGATTAGGAAGTCATGGAGCCGCTGGACACTGGCGTaG SEQ ID NO:38
    V Q A E I R K S W S R W T L A * SEQ ID NO:39
  
```

Figure 10

## MAP of rdel (Nt/Ct)

a ATGGGGGCGCCCGGATCGCAOCCAGCCTGGCGCTCCTACTCTGCTGCCCCAGTGCTCAGC  
 M G A A R I A P S L A L L L C C P V L S -  
 a TCCGCATATGCGCTGGAGGTATTTGACCGCCTAGGCATGATCTACACCGTGGGATACTCC  
 S A Y A L E V F D R L G M I Y T V G Y S -  
 a ATGTCTCTCGCCTOCCCTCACGGTGGCTGTGCTCATCCTGGCCTATTTTAGGGCGCTGCAC  
 M S L A S L T V A V L I L A Y F R R L H -  
 a TGCACGCGCAACTACATCCACATGCACATGTTCTGTCGTTATGCTGGCGCGCGGAGC  
 C T R N Y I H M H M F L S F M L R A A S -  
 a ATCTTCGTGAAGGAAGCTGTGCTCTACTCTGGCTTCACGCTGGATGAGGCCGAGCGCCTC  
 I F V K D A V L Y S G F T L D E A E R L -  
 a ACAGAGGAAGAGTTGCACATCATCGCGCAGGTGCCACCTCCGCCGGCGCGCTGCCGCCGTA  
 T E E E L H I I A Q V P P P P A A A A V -  
 a GGCTACGCTGGCTGCCCGGTGGCGGTGACCTTCTTCCTCTACTTCCTGGCTACCAACTAC  
 G Y A G C R V A V T F F L Y F L A T N Y -  
 a TACTGGATCTGGTGGAGGGGCTGTACTTGCACAGCCTCATCTTCATGGCCTTTTCTCA  
 Y W I L V E G L Y L H S L I F M A F F S -  
 a GAGAAGAAGTACCTGTGGGGCTTCACCATCTTTGGCTGGGGTCTACCGGCTGTCTTCGTG  
 E K K Y L W G F T I F G W G L P A V F V -  
 a GCTGTGTGGTGGTGTGAGCAACCTTGGCCAACACTGGGTGCTGGGATCTGAGCTCC  
 A V W V G V R A T L A N T G C W D L S S -  
 a GGGCACAAGAAGTGGATCATCCAGGTGCCCATCCTGGCATCTGTTGTGCTCAACTTCATC  
 G H K K W I I Q V P I L A S V V L N F I -  
 a CTTTTATCAACATCATCCGGGTGCTTGCCACTAAGCTTCGGGAGACCAATGCGGGCCGG  
 L F I N I I R V L A T K L R E T N A G R -  
 a TGTGACACCAGGCAGCAGTACCGGAAGCTGCTCAGGTCCACGTTGGTCTCGTCCCGCTC  
 C D T R Q Q Y R K L L R S T L V L V P L -  
 a TTTGGTGTGCACTACACCGTCTTCATGGCCTTGCCGTACCCGAGGTCTCAGGGACATTG  
 F G V H Y T V F M A L P Y T E V S G T L -  
 a TGGCAGATCCAGATGCATTATGAGATGCTCTTCAACTCCTTCCAGGGATTTTGTGTC  
 W Q I Q M H Y E M L F N S F Q G F F V A -  
 a ATCATATACTGTTTCTGCAATGCTGAGGTGCAGGCAGAGATTAGGAAGTCATGGAGCCGC  
 I I Y C F C N G E V Q A E I R K S W S R -  
 a TGGACACTGGCGT<sub>a</sub>g SEQ ID NO: 40  
 W T L A \* SEQ ID NO: 41

# FIGURES 11A-11D

Oligo is designed to join PTH(1-9) sequence to core of receptor using a Gly linker. Test for constitutive activation.  
Insert immediately after predicted signal peptidase cleavage site (Tyr23, use Ala24 as Ala1 of PTH. Join to Glu-182, - boundary of exonC/H1.  
KHA.WT map red - flanking homology

(1-40)

ATGGGGGGGGGGGGGATCGCACCCAGCCTGGCGCTCTACTCTGCTGCCAGTCTCTCAGC  
M G A A R I A P S L A L L L C C P V L S -

SEQ ID NO: 46 and 53.

NDEI--

TCCGCATATGGCTGGTGGACGGACGATGCTTTACCAAAGAGGAACAGATTTTCCTG  
S A Y A L V D A D D V F T K E E Q I F L -

FIG. 11 A

(161-200)

AACCGGACGTGGGGCAACTACAGCGAGTGCCTCAAGTTCATGACCAATGAGACCGGGAA  
553 N R T W A N Y S E C L K F M T N E T R E - 612  
CGG GAGGTATTTGACCGCCTAGGCATGATCTACACCGTGGGATACTCCATGCTCTCTCCG  
613 R E V F D R L G H I Y T V G Y S H S L A - 672

SEQ ID NO 47 and 54

Backtranslate PTH(1-9) Gly4.:

CCUGUUUCCGAAAUCCAGCUGAUGCACggcgaggagggc

SEQ ID NO 48

Insert PTH(2-9).Gly4 between A24 and E182, use about 30 nts for flanking homology  
5' flank Hom - 33 nt, 3' flank Hom - 30 nt, total - 99 nts.

Oligo: Sequence ID#: E16631A1

CTCTGCTGCCAGTCTCTCAGCTCCGCTATCGCGTTTCCGAAATCCAGCTGATGCACggcgaggagggc  
GAGGTATTTGACCGCCTAGGCATGATCTAC

SEQ ID NO 49

CCG check:

MAP of: Y23E182G4PTH1-9.seq from: 1 to: 99

DNA sequence for making Tethered PTH ligand/receptor

Receptor - rat PTH1 Rec

Insert PTH(1-9)-Gly4 sequence between Tyr23 and Glu182.

Use Ala24 as codon 1 of PTH, flanking homology of ~30 nts

Takes out NDEI site at Ala 22 CCA->GCC

With 1 enzymes: NDEI

FIG 11 B

FIG. 11 C

CTCTGCTGCCAGTCTCTCAGCTCCGCTATCGCGTTTCCGAAATCCAGCTGATGCACgggc  
L C C P V L S S A Y A V S E I Q L M H G -  
ggaggaggcGAGGTATTTGACCGCCTAGGCATGATCTAC  
G G G E V F D R L G H I Y -

SEQ ID NO: 50 and 55

FIG. 11 D

Helix II: -/rec-dna> more tether-1.map from: 2350 to: 2650

tethered PTH(1-9) to core receptor.

PTH(1-9) linked to Glu-182 of rat receptor.

insert immediately after Tyr23 cleavage site.

ligo tether 1 spans 2358 to 2891.

Takes out NDEI at 2390 Ala-22).

FIG. 11.E

NdeI CA'TA\_TG Cuts at: 1790 1790  
Size: 5769

MAPSORT of: rDeleI-G.seq from: 1. to: 5736

\*\*\*To be used as template SS DNA for Tether-1 OH.

With 1 enzymes: NDEI

NdeI CA'TA\_TG

Cuts at: 1790 2384 1790  
Size: 594 5142

(1-40)

Oligo Mini-HA-1:

Sequence ID#: E16853A1

CTCTGCTGCCAGTGCTCACTCCGCATATccctacgacgtccccgactacgccggcgaggaggcgAGGTATTTGACCGCCTAGGCATGATCTAC

SEQ ID NO 51

FIG 11.F

MAP of: mini-HA.seq from: 1 to: 96  
Oligo sequence for adding HA Epitope tag to Headless rat P1R.  
Insert 9 aa tag, YPYDVPDYA, between Tyr23 and Glu182, using  
Tyr 23 as codon 1 of tag, and add 4 glys for spacer. Flanking homology of -30  
nts. Takes out NDEI site at Ala 24 GCG->ccc (31-33).

With 1 enzymes: NDEI

1 CTCTGCTGCCAGTGCTCACTCCGCATATccctacgacgtccccgactacgccggcgaggaggcgAGGTATTTGACCGCCTAGGCATGATCTAC 60

SEQ ID NO: 52 and 56

A L C C P V L S S A Y P Y D V P D Y A G G -

61 ggaggcgAGGTATTTGACCGCCTAGGCATGATCTAC 96

FIG 11.G

A G C E V F D R L G H I Y -

Enzymes that do not cut: NdeI

Fig 12

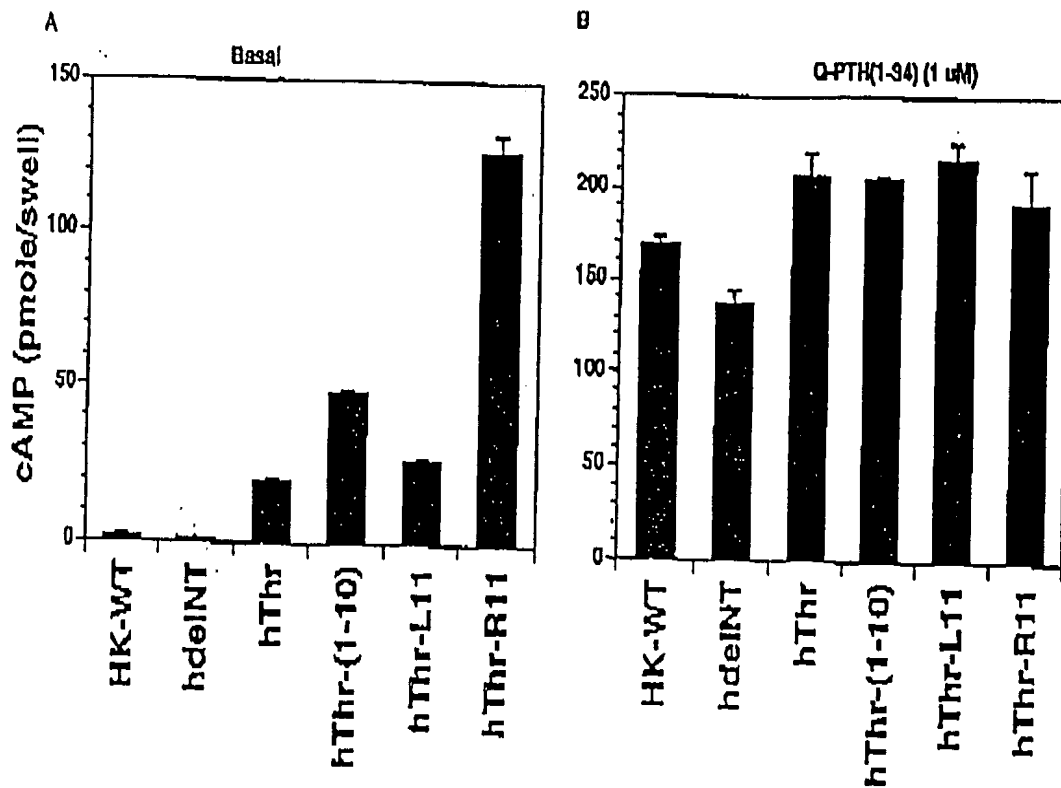


Fig 13

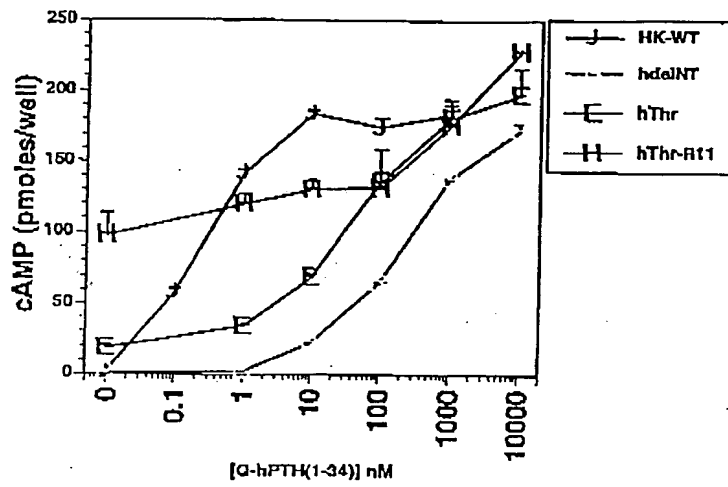


Fig 4

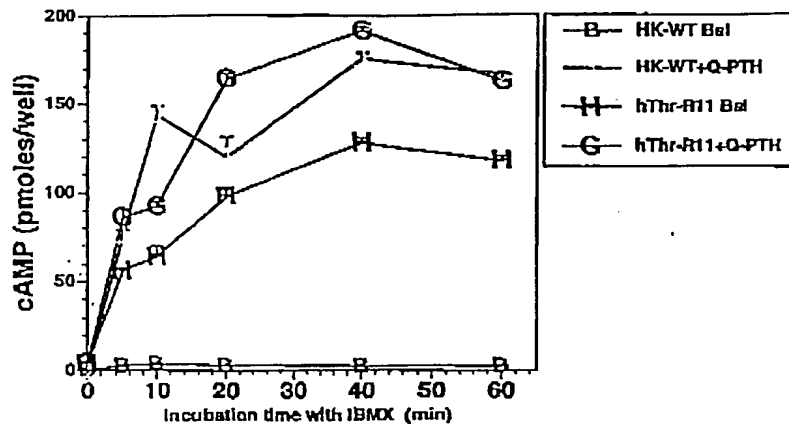


Fig 13

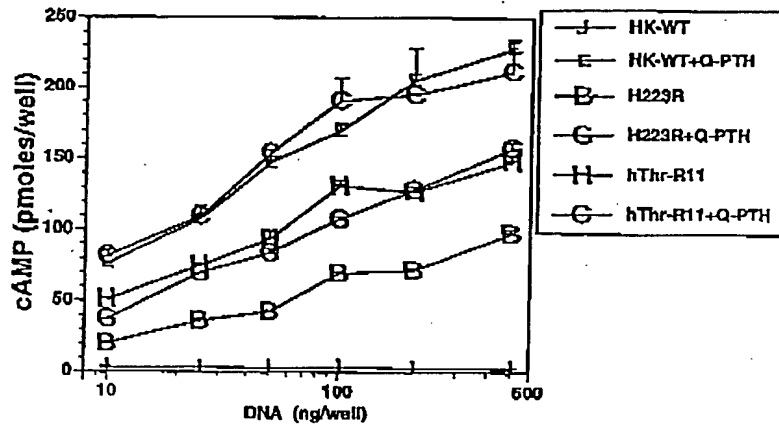




Fig 16

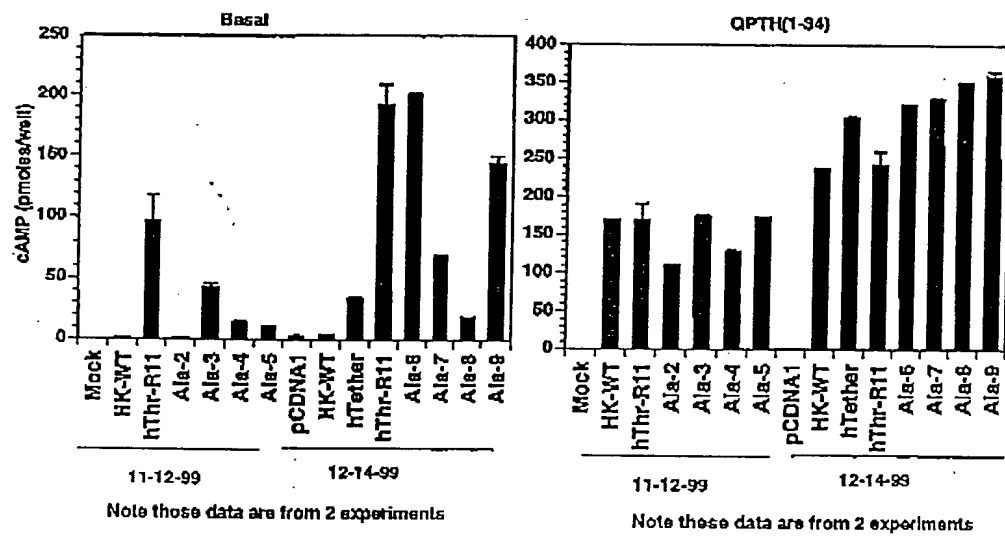


FIGURE 17

**hTether-1** From human PTH-1 receptor by replacing Ala24 to Arg181 with Ala1 to His9 of PTH, then 4-Gly linker between His9 and Glu182 by oligonucleotide mutagenesis with oligo E20986

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2287  atggggAaccGccggatcgacacccggcctggcgctcctgctctgctgccccgtgctcagc
a      M G T A R I A P G L A L L L C C P V L S 2346
      tccgcgtacgcgggtttccgaaatccagctgatgcacggcgaggaggogaggtgtttgac
2347  a      S A Y A V S E I Q L M H G G G G E V F D 2406
      cgccctgggcatgatttacaccgtgggctactccgtgtccctggcgtccctcaccgtagct
2407  a      R L G M I Y T V G Y S V S L A S L T V A 2466
      gtgctcatcctggcctactttagggcggtgcactgcacgcgcaactacatccacatgcac
2467  a      V L I L A Y F R R L H C T R N Y I H M H 2526
      ctgttctctgtccttcatgtgcgcgcggtgagcatcttcgtcaaggacgctgtgtotao
2527  a      L F L S F M L R A V S I F V K D A V L Y 2586
      tctggcgccacgcttgatgaggctgagcgccctcaccgaggaggagctggcgccatcgcc
2587  a      S G A T L D E A E R L T E E E L R A I A 2646
      caggcgcccccgccgctgcccaccgcgctgcccgtacgcgggtgcagggtggctgtg
2647  a      Q A P P P P A T A A A G Y A G C R V A V 2706
      accttcttcttcttcttcttggccaccaactactactggattctgttggagggtgtac
2707  a      T F F L Y F L A T N Y Y W I L V E G L Y 2766
      ctgcacagcctcatcttcatggccttcttctcagagaagaagtacgtggggcttcaca
2767  a      L H S L I F M A F F S E K K Y L W G F T 2826
      gtcttcgggtgggtctgcccgtgtcttcgtggctgtgtgggtcaggtgcagagctacc
2827  a      V F G W G L P A V F V A V W V S V R A T 2886
      ctggccaacacgggtgctgggacttgagctccgggaacaaaaagtggatcatccagggtg
2887  a      L A N T G C W D L S S G N K K W I I Q V 2946
      cccatcctggcctccattgtgtcctaacttcatcctcttcatcaatatcgtccgggtgctc
2947  a      P I L A S I V L N F I L F I N I V R V L 3006
      gccaccaagctgcgggagaccaacgcggcggtgtgacacacggcagcagtagccggaag
3007  a      A T K L R E T N A G R C D T R Q Q Y R K 3066
      ctgctcaaatccacgctggtgctcatgccccctcttggcgctccactacattgtcttcacg
3067  a      L L K S T L V L M P L F G V H Y I V F M 3126
      gccacaccatacacggaggtctcagggacgctctggcaagtcagatgcactatgagarg
3127  a      A T P Y T E V S G T L W Q V Q M H Y E M 3186
      ctcttcaactccttccagggttttttgtcgcaatcataactgtttctgcaatggcgag
3187  a      L F N S F Q G F F V A I I Y C F C N G E 3246
      gtacaagctgagatcaagaaatcttggagccgctggacactggcactggacttcaagcga
3247  a      V Q A E I K K S W S R W T L A L D F K R 3306
      aaggcagcgagcgggagcagcagctatagctacggccccatggtgtccacacaggtgtg
3307  a      K A R S G S S S Y S Y G P M V S H T S V 3366
      accaatgtcgcccccggtgtggactcggcctgccccctcagcccccgctactgcccact
3367  a      T N V G P R V G L G L P L S P R L L P T 3426
      gccaccaccaacggccaccctcagctgcctggccatgccaaagccagggaacccagccctg
3427  a      A T T N G H P Q L P G H A K P G T P A L 3486
      gagaccctcgagaccacaccctgccatggctgtctcccaaggacgatgggttctcaac
3487  a      E T L E T T P P A M A A P K D D G F L N 3546
      ggctcctgtcaggcctggacgaggagcctctgggcctgagcggccacctgcccctgcta
3547  a      G S C S G L D E E A S G F E R P P A L L 3606
      cagggaaggtgggagacagtcatgtgaccaggcgctgggggct
3607  a      Q E E W E T V M - 3649

```

SEQ ID NO: 61  
SEQ ID NO: 62

FIGURE 18

## hdeLNT

human PTH-1 rec deleted for 24-181; Joins Tyr23 to Glu182.  
February 25, 1999 13:38 ..

SEQ 10 NO: 59.

SEQ ID NO: 60

[illegible]

FIGURE 19

hTether-R11

Made from hTether-1 by inserting Asn10-Arg11 between His9 and first Gly of linker by oligonucleotide mutagenesis with Oligo - E27309

	atgggGACcGccggatcgacccggcctggcgctcctgctctgctgccccgtgctcagc	2287	SEQ ID NO: 57
a	M G T A R I A P G L A L L L C C P V L S	2346	SEQ ID NO: 58
	tcgcgtacgcgggtttccgaaatccagctgatgcaTAATCGTggcggaggaggcgaggtg		
a	S A Y A V S E I Q L M H N R G G G G E V	2406	
	tttgaccgcctgggcatgatttacaccgtgggctactccgtgtccctggcgctccctcacc		
a	F D R L G M I Y T V G Y S V S L A S L T	2466	
	gtagcgtgctcctcctggcctacttttagcggtgcaactgcacgcgaactacatccac		
a	V A V L I L A Y F R R L H C T R N Y I H	2526	
	atgcaccgttccctgtccttcctgctgctgcgcgcctgagcatcttcgtcaaggacgctgtg		
a	M H L F L S F M L R A V S I F V K D A V	2586	
	ctctactctggcgccacgccttgatgaggtgagcgccctaccgaggaggagctgcgcgcc		
a	L Y S G A T L D E A E R L T E E E L R A	2646	
	atgcgccaggcgccccgcgcgcctggcaccgcgcgtgcccggctacgcgggtgcagggtg		
a	I A Q A P P P P A T A A A G Y A G C R V	2706	
	gctgtgaccttcttcttcttcttctggccaccaactactactgattctggtggagggg		
a	A V T F F L Y F L A T N Y Y W I L V E G	2766	
	ctgtacctgcacagcctcatcttcatggcctcttctcagagaagaagtacctgtggggc		
a	L Y L H S L I F M A F F S E K K Y L W G	2826	
	ttcacagtcttcggctggggtctgcccgtgtcttctggtgtgtgggtcagtgctaga		
a	F T V F G W G L P A V F V A V W V S V R	2886	
	gctaccctggccacacccgggtgctgggacttgagctccgggaacaaaaagtggtatc		
a	A T L A N T G C W D L S S G N K K W I I	2946	
	cagggtgccatccctggcctccattgtgctcaacttcctcttcatcaatatcgtccgg		
a	Q V P I L A S I V L N F I L F I N I V R	3006	
	gtgctcgccaccaagctgcgggagaccaacgcggcgggtgtgacacacggcagcagtac		
a	V L A T K L R E T N A G R C D T R Q Q Y	3066	
	cggaagctgctcaaatccacgctggtgctcatgccctcttggcgctccactacattgtc		
a	R K L L K S T L V L M P L F G V H Y I V	3126	
	ttcatggccacacacacacgggtctcaggagcgtctggcaagtccagatgcactat		
a	F M A T P Y T E V S G T L W Q V Q M H Y	3186	
	gagatgctcttcaaotccttccagggtatrtttgtgcgaatcatatactgtttctgcaat		
a	E M L F N S F Q G F F V A I I Y C F C N	3246	
	ggcgaggtacaagctgagatcaagaaatcttggagccgctggacactggcactggacttc		
a	G E V Q A E I K K S W S R W T L A L D F	3306	
	aagcgaaaggcagcagcgggagcagcagctatagctacggcccatggtgtccacaca		
a	K R K A R S G S S S Y S Y G P M V S H T	3366	
	agtgtgaccaatgtcggccccgtgtgggactcggcctgccccacagccccgcctactg		
a	S V T N V G P R V G L G L P L S P R L L	3426	
	ccactgccaccaccaacggccaccctcagctgcccggccatgccaagccagggaaccca		
a	P T A T T N G H P Q L P G H A K P G T P	3486	
	gccctggagaccctcgagaccacaccacctgccatggctgctcccaaggacgatgggttc		
a	A L E T L E T T P P A M A A P K D D G F	3546	
	ctcaacggctcctgctcaggcctggacgaggaggcctctgggctgagcgccactgccc		
a	L N G S C S G L D E E A S G P E R P P A	3606	
	ctgctacaggaagagtgggagacagtcattgtgaccaggcgtgggggctggacctgctga		
a	L L Q E E W E T V M *	3666	